REMARKS

PRIORITY DATA

The Examiner has stated that the current application is not a continuation of U.S. Patent Application Serial Nos. 09/373,337, 08/794,970, 08/645,826 and 08/202,505. The Examiner is directed to the granted petition accepting Applicants' claim for priority wherein priority to the above-mentioned applications is properly claimed.

The Examiner has repeated the below objections/rejections in various Office Actions. Applicant has presented arguments in response to these objections/rejections on numerous occasions, but the Examiner has not responded to these arguments. In a telephone conversation with the Examiner and his supervisor on December 10, 2007, the undersigned was assured that the Examiner would consider and respond to Applicants' arguments, which are repeated below.

It should be noted that in a previous amendment, Applicant has added the term comprising "the steps of" in order to clarify that the inventions set forth in Claims 99 and 115 are for a "method" and not an "apparatus". Applicant has deleted that phrase in this amendment to ensure that the Claims are copied verbatim from U.S. Patent No. 6,285,027 in order to provoke an interference therewith. For the reasons set forth below Applicant believes that Claims 99 and 115 are fully supported by instant Specification and by that of U.S. Patent No. 5,689,111 of which the current application is a continuation. Applicant therefore maintains that the current application is in interference with U.S. Patent No. 6,285,027.

OBJECTED DRAWINGS

The drawings were objected to for not showing every feature of the invention specified in the Claims. Applicant traverses the Examiner's objection. The claims pending in the application are method Claims. As such there is no

particular feature or device that "provides a delay between the release of the pulses of trapped ions and initiation of pulses ..." Rather such delay is achieved by practicing the method of the invention as illustrated below The same is true for "adjusting the delay to improve the duty cycle efficiency of ions ..." Applicant notes that the Examiner refers to the above-mentioned steps as a "*means* for providing..." and a "*means* for adjusting." However, Applicant claims a method comprising "[*the step* of] adjusting" and "[*the step* of] providing" and not *a means* of "adjusting" and "providing." The claimed invention is not limited to any particular device or apparatus. Applicant additionally takes note of the comments made in the 35 USC 112 rejection in which the Examiner asks "what is the *device* that is used to adjust the delay..."

REJECTION UNDER 35 USC 112 FIRST PARAGRAPH

Step (e) of claims 99 and 115 is for "providing a delay between the release of the pulses in the time of flight instrument, and adjusting the delay to improve the duty cycle efficiency of ions with the second mass-to-charge ratio." The Examiner has rejected Claims 99 and 115 because Step (e) was not adequately described in the Specification. Applicant traverses this rejection by pointing out to the Examiner where support for Step (e) is found in the Specification of the current application and in U.S. Patent No. 5,689,111 (hereinafter '111) of which the current application is a continuation.

Support for step (e) is found initially in the instant specification pg. 24, lines 8-10 which state:

> "Instead, trapping and the timed release of ions from the multipole ion guide is a preferred method for improving duty cycle."

This teaching introduces the concept of improving the duty cycle by a process of trapping ions and properly timing their release to the TOF. This concept is elaborated, following a detailed discussion of different ways of

performing the trapping step in a subsequent passage on pg. 26, line 6 – pg. 27, line 5.

> "By either trapping method, ions continuously enter ion guide 16 even while ion packets are being pulsed out exit end 24. The time duration of the ion release from ion guide exit 24 will create an ion packet 52 of a given length as diagrammed FIG. 2. As this ion packet moves through lenses 27 and into pulsing region 30 some m/z TOF partitioning can occur as diagrammed in FIG. 3. The m/z components of ion packet 52 can occupy different axial locations in pulsing region 30 such as separated ion packets 54 and 56 along the primary ion beam axis. Separation has occurred due to the velocity differences of ions of different m/z values having the same energy. The degree of m/z ion packet separation is in part a function of the initial pulse duration. The longer the time duration that ions are released from exit 24 of ion guide 16, the less m/z separation that will occur in pulsing region 30. All or a portion of ion packet 52 may fit into the sweet spot of pulsing region 30. Ions pulsed from the sweet spot in pulsing region 30 will impinge on the surface of detector 38. If desired, a reduced m/z range can be pulsed down flight tube 42 from pulsing region 30. This is accomplished by controlling the length of ion packet 52 and timing the release of ion packet 52 from ion guide 16 with the TOF pulse of lenses 34 and 35. A time separated m/z ion packet consisting of subpackets 54 and 56 just before the TOF ion pulse occurs is diagramed in FIG. 3. Ion subpacket 56 of lower m/z value has moved outside the sweet spot and will not hit the detector when accelerated down flight tube 42. Ion subpackets 57, originally subpackets 54, are shown just after the TOF ion pulse occurs. These subpackets will successfully impinge on detector 38. The longer the initial ion packet 52 the less mass range reduction can be achieved in pulsing region 30. With ion trapping in ion guide 16, high duty cycles can be achieved and some degree of m/z range control in TOF analysis can be achieved independent or complementary to mass range selection operation with ion guide 16."

This passage first describes a pulse, or packet, of ions of a given length (depending on the trap pulse duration) being pulsed out of the ion guide trap. Then, "As this ion packet moves through lenses 27 and into pulsing region 30 some m/z TOF partitioning can occur..." (pg 26, line 8). In other words, it takes some time for the pulsed ion packet to travel from the ion guide trap to the pulsing region of the TOF, and, obviously, the TOF push-pull pulse would not be activated until the ion packet, or some portion of the packet, has arrived within the TOF 'sweet spot', that is, the region within the TOF pulse region from which ions are able to reach the TOF detector once the TOF pulse occurs. This time delay is expressed explicitly in this passage by "...timing the release of ion packet 52 from ion guide 16 with the TOF pulse of lenses 34 and 35. A time separated m/z ion packet consisting of subpackets 54 and 56 just before the TOF ion pulse occurs is diagramed in FIG. 3." (pg 26, line 19). '...Timing the release of ion packet...with the TOF pulse...' is the same as 'providing a delay between the trap release of the pulses of trapped ions and the initiation of push-pull pulses in the time of flight instrument' because timing release of individual packets inherently has a delay between successive individual packets. Such a delay is even more explicitly described in the '111 description, as discussed below

The second part of step (e) is '...and adjusting the delay to improve the duty cycle efficiency of ions with the second mass-to-charge ratio'. The passage from the instant application quoted above includes the statements: "All or a portion of ion packet 52 may fit into the sweet spot of pulsing region 30. Ions pulsed from the sweet spot in pulsing region 30 will impinge on the surface of detector 38." In other words, this passage teaches that all ions of an ion packet may be detected in the TOF, provided that they are located within the sweet spot of the TOF pulsing region at the time that the TOF pulse occurs. Now, as is known to one of skill in the art, all ions of an ion packet of a particular mass-to-

charge ratio will be located within the sweet spot of the TOF pulsing region only if the timing of the TOF pulse occurs after a particular time delay relative to the ion guide trap release pulse. Hence, it would seem to be clear that this passage supports the second part of step (e) '... adjusting the delay to improve the duty cycle efficiency of ions with the second mass-to-charge ratio'.

The above arguments for support for step (e) are further bolstered by considering the U.S. Patent No. 5,689,111, which describes in explicit detail the pulsed release of ions from an ion guide trap, and the improvement in duty cycle of an ion with a particular mass-to-charge ratio by adjusting the delay between the release of the pulses of trapped ions and initiation of TOF pulses. In the '111 description, Col. 8, lines 1-28 read:

> "As an example to the ion storage mode of operation, let us again use the same mixture of ions M1, M2, and M3 of ionic masses 997, 508 and 118 as used above in continuous mode of operation. As shown in FIG. 4, and FIG. 6 the pulsed ion beam of duration t1 from the region 72 is injected between the parallel plates 23 and 24 when the plates are initially held at the absence of an electric field, i.e. voltage level 79 on the repeller lens 23. According to the above equation (3), lighter ions moving faster than the heavier ions, the three masses will start to separate from each other in the region 26. After a certain variable delay t2, the electric field in the region 26 is pulsed on for a short period of time t3 by the repeller plate 23. The delay time t2 can be changed to allow different sections of the original ion beam, i.e. different m/z packages, to accelerate perpendicular to their original direction towards the flight tube 35 to be detected for mass analysis. In this example, a delay time t2 was chosen to pulse only a narrow range of ions centered around mass (M2) 53 which were accelerated in the direction 63 at the instant the field was turned on. At the same instant, both the masses M1 52 and M3 54 will hit the sides of the lenses moving in the approximate direction 62 and 64 and will not be detected by the mass analyzer."

This passage describes 'providing a delay (i.e , t2) between the release of the pulses of trapped ions and initiation of push-pull pulses in the time of flight instrument,' in the passage "After a certain variable delay t2, the electric field in the region 26 is pulsed on" , while 'and adjusting the delay to improve the duty cycle efficiency of ions with the second mass-to-charge ratio' is described by "..delay time t2 can be changed to allow.. different m/z packages.. to be detected for mass analysis.. a delay time t2 was chosen to pulse only a narrow range of ions centered around mass (M2) 53...". The resulting improvement in the duty cycle is demonstrated in the subsequent description of demonstrated experimental results in Col. 8, lines 44-67 through Col 9, lines 1-16, which read:

> "FIGS. 7A and 7B show the actual experimental results acquired using both the continuous and ion storage mode of operations for a sample using a mixture of ions used in the above examples. The actual sample was a mixture of three compounds Valine, tri-tyrosine, and hexa-tyrosine. Upon electrospray ionization of this mixture, the predominant molecular ions with nominal masses 118, 508, and 997 are generated in the ionization source 10. The bottom trace of FIG. 7A shows all three of these ions detected and registered as peaks 73, 71, and 74 when the mass spectrometer was in the continuous mode of operation. The top trace mass spectrum in FIG. 7A shows the results when the mass spectrometer was changed to the ion storage mode of operation. Both modes were acquired in similar experimental conditions. The acquisition rate i.e. the repetition rate counted by the repeller lens was 8200 per second. Each trace represents 4100 full averaged scans. As seen from the top spectral trace, there is only one predominant registered peak 72 in the spectrum. This peak corresponds to a molecular ion 508 enhanced in signal strength by about a factor of ten with respect to the peak 71 in continuous mode of operation. For the reasons explained in above examples, both of the molecular ions 118 and 997 are absent from the ion storage mode spectral trace as expected. The signal intensity increase comes from the fact that all of the ions that would otherwise be

> lost in the continuous ion mode were actually being stored in the ion guide for the next scan. According to the above example, for the continuous mode of operation, the approximate duty cycle calculated for the 508 peak at 8,200 scans/s would be 9% i.e. one out of every twelve ions being detected. As the experimental results suggest in the ion storage mode of operation at 8,200 scans/s in FIG. 7A, most of the lost ions predicted in the continuous ion mode were recovered.

This passage demonstrates a molecular ion 508 enhanced... signal strength by about a factor of ten with respect to the peak 71 in continuous mode of operation ... when the mass spectrometer was changed to the ion storage mode of operation, that is, as described in the previous passage, by providing a delay between the trap release and the TOF pulse and adjusting the delay to maximize the intensity of the m/z 508 ion, resulting from an improvement in duty cycle relative to continuous beam operation.

Hence, there is sufficient support for step (e) in the current description only, and even stronger support when considering the description of parent patent '111.

While the explicit description of the method step (e) is discussed in detail in the May 19, 2004 Response, as reiterated above, the means for performing this method step (e) is further described explicitly in the '111 patent, col. 7, line 59 through col. 8, line 6:

> "FIG. 6 shows the driving mechanism and the timing sequence between the ion guide exit lens 15 and the time-of-flight repeller lens 23 for a single cycle, i.e. a single mass spectral scan. The trace 83 shows the ion guide exit lens voltage status switching between the two voltage levels 77 and 78 and the trace 82 shows the repeller lens voltage status switching between the two levels 79 and 80. The power supply 91 sets the desired upper and lower voltage levels to be delivered to the lenses at all times. The electrically isolated fast switching circuitry 92 controls

synchronously the desired voltage levels of the lens electrode 15 and the repeller plate 23 to be switched back and forth during the designated time intervals controlled by the pulse and delay generating device 93, which is an accurate timing device, which in turn is controlled by the user interface."

In particular, this passage teaches explicitly that "a pulse and delay generating device 93 ... controlled by the user interface" is the means used to adjust the delay.

REJECTION UNDER 35 USC 102(e)

Claims 99 and 115 have been rejected as being clearly anticipated by Chernuvich et al. (6,285,027). It is for this reason that Applicant believes that an interference should be declared between the current application and the above-cited patent.

SUMMARY

Claims 99 and 115 are supported by the specification of this application Serial No. 09/901,428. Further, the Claims are unequivocally supported in parent patent '111. As to the rejection of the Figures, it is submitted that such rejection has also been overcome since the specification teaches one of ordinary skill in the art to practice the steps of the method. Nothing more need be added to the drawings.

In light of the above argument and amendment, Applicant believes that an interference should be declared.

Respectfully submitted,

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